

III. REMARKS

The final Office Action dated October 1, 2008, has been received and carefully noted. The above amendments and replacement drawings, and the following remarks are being submitted as a full and complete response thereto.

Claims 1-4 and 6-24 are pending.

By this Amendment, claims 1, 3, 4, 6-7, 9, 14, 16-17, 19, 21, 23, and 24 are amended, and claim 2 is canceled. Support for the amendments may be found in the specification and claims as originally filed. Claims 1-4, 6-7, 9, and 19 have been amended to clarify the scope of the presently claimed invention. Claim 24 has been amended to correct a typographical error. Support for the amendment to claim 1 can be found in canceled claim 2 and in the specification at least on page 4, lines 13-19. Support for the amendments to the claims 14, 16, and 17 can be found in the specification at least on page 3, lines 22-26, and page 7, lines 2-7. Support for the amendment to claim 21 can be found in the specification at least on page 7, lines 8-25. Support for the amendment to claim 23 can be found at least on page 8, lines 4-15. Applicants submit that no new matter is added. Applicants respectfully request reconsideration and withdrawal of all objections and rejections

Entry of this Amendment is proper under 37 C.F.R. § 1.116 since this Amendment: (a) places the application in condition for allowance for reasons discussed herein; (b) does not raise any new issues regarding further search and/or consideration since the Amendment amplifies issues previously discussed throughout prosecution; (c) does not present any additional claims without canceling a corresponding number of

finally-rejected claims, and (d) places the application in better form for appeal, should an appeal be necessary. Entry of this Amendment is thus respectfully requested.

Drawings

The Examiner has objected to the drawings, asserting that Figures 1-5 are difficult to read. Applicants have submitted replacement drawings and accordingly, request withdrawal of the objection to the drawings.

Objections to the Claims

Claims 2-4, 19, 21, and 23 were objected to because of the asserted formalities.

Claim 2 has been canceled. Applicants have amended claims 3, 4, 19, 21, and 23 in accordance with the Examiner's suggestions. Accordingly, Applicants respectfully request withdrawal of the objection to claims 2-4, 19, 21 and 23.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-4 and 6-24 were rejected under 35 U.S.C. § 112, second paragraph, for the asserted indefiniteness. Applicants traverse the rejection.

Regarding the rejection of claim 1, the Examiner has asserted that the phrase "a region of Obelin protein with a corresponding region of Clytin photoprotein, wherein said region is located between residue 42 and 122 of the Obelin protein sequence (SEQ ID NO:2)" in claim 1 is unclear and indefinite. In particular, the Examiner states that it is unclear how regions of Obelin and Clytin photoproteins correspond to each other

(whether they correspond structurally, functionally, or both, and under what criteria).

Applicants submit that "corresponding region" is defined in the specification as follows:

A "corresponding region or fragment", as used herein, means any amino acid sequence, within the selected photoprotein, matching Obelin sequence in respective sequence alignments with the exception of at least 1, preferably at least 5, more preferably at least 10 amino acid residues, which are not conserved in the relevant proteins (Obelin and selected photoprotein), said region or fragment preferably spanning residues 42-122, more preferably residues 50-95, as referred to Obelin sequence.

(specification, page 4, lines 13-19).

For further clarification, Applicants have enclosed two Figures showing the alignments between the Obelin and Clytin sequences. Both figures designate, by boxes, the region spanning residues 42-122, and the grey letters in the second figure show the mismatches.

Regarding the rejections of claims 2-4, 6, 7, and 9, Applicants have canceled claim 2 and amended the claims 3, 4, 6, 7, and 9 to address the Examiner's concerns. In particular, claims 3 and 4 have been amended to eliminate the phrase "the selected photoprotein." Claims 6, 7, and 9 have been amended to recite particular sequence numbers.

For at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-4 and 6-24 under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 112, first paragraph

1. Written Description

Claims 1-4 and 6-24 were rejected under 35 U.S.C. §112, first paragraph, for the asserted failure to comply with the written description requirement. Applicants traverse the rejection.

In particular, the Examiner asserts that the “genus of claimed chimeric photoproteins are not limited with respect to its structure and function” and that the genus “includes a chimeric photoprotein obtained by replacing any region with any fragment of Clytin photoprotein, wherein said genus does not have to have any desired biological function.” The Examiner also asserts that the specification does not provide adequate written description with respect to how such a broad genus of structures correlates with biological function, as the Examiner states that the specification discloses only a single representative species of a chimeric photoprotein comprising the amino acid sequence as set forth in SEQ ID NO:3.

Applicants note that claim 1 has been amended to specify that the “chimeric photoprotein [is] obtained by replacing a region of Obelin protein of SEQ ID NO:2 with a corresponding region on Clytin photoprotein, wherein said region is located between residue 42 and 122 of SEQ ID NO:2, wherein said chimeric photoprotein is bioluminescent...” (emphasis added). Applicants note that claim 1 has been further amended to incorporate the limitations of canceled claim 2, and recites that the “corresponding region of Clytin photoprotein is identical to said region of Obelin protein sequence that is to be replaced with the exception of at least 1 amino acid residue.”

Applicants submit that the presently amended claims are directed to a specific region (a region between residue 42 and 122) of the specific Obelin protein sequence of SEQ ID NO:2, and therefore the genus of claimed chimeric photoproteins are limited with respect to its structure and function. Further, Applicants submit that the presently amended claims require that the chimeric photoproteins have the biological function of bioluminescence.

For at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-4 and 6-24 under 35 U.S.C. § 112, first paragraph, for the asserted failure to comply with the written description requirement.

2. Enablement

Claims 1-4 and 6-24 are rejected under 35 U.S.C. § 112, first paragraph, for the asserted failure to comply with the enablement requirement. Applicants traverse the rejection.

Applicants respectfully disagree with the Examiner's assertions. For example, Applicants disagree with the Examiner's assertion that there would be undue experimentation for one skill in the art to make any chimeric photoprotein by replacing any region of Obelin with any fragment of Clytin in order to obtain photoproteins that retain the desired biological function. Applicants note that the amended claims are limited to a specific region (between residues 42 and 122) of a specific protein sequence (the Obelin sequence of SEQ ID NO: 2).

Furthermore, Applicants note that the chimeric photoprotein of the present invention "produces an intense bioluminescence in response to calcium stimulation,

which is generally higher than that observed with natural photoproteins" (see specification, page 5, lines 3-5). In other words, Applicants submit that the modifications introduced in the Obelin molecule determine a functional change in terms of bioluminescence emission, which is higher than that produced by natural proteins. As a consequence of this functional improvement, Applicants submit that the chimeric protein may be conveniently used in several applications, for example, in methods for detecting calcium ions or for screening of biologically active molecules. Applicants submit that the preparation of chimeric proteins included in the present claims is well within the competence of one of ordinary skill in the art, who may find adequate guidance in the specification, see in particular pages 5 and 6. Applicants submit that by replacing a fragment of Obelin sequence within the first two calcium binding sites (i.e. in the identified region), with a fragment of Clytin, which in respective sequence alignment corresponds to the former fragment with at least one mismatch, as recited in presently amended claim 1, a chimeric photoprotein is produced which not only retains biological function, but is able to emit a more intense luminescence upon calcium binding than the corresponding natural proteins.

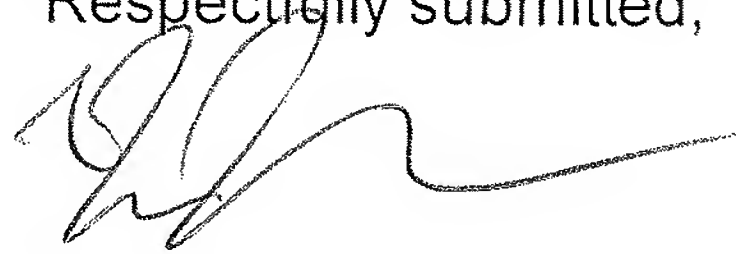
For at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-4 and 6-24 under 35 U.S.C. § 112, first paragraph, for the asserted lack of enablement.

IV. CONCLUSION

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

In the event that this paper is not being timely filed, Applicants respectfully petition for an appropriate extension of time. Any fees for such an extension, together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account Number 01-2300, referencing Docket Number 100506-00025.

Respectfully submitted,



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Enclosures: Replacement Figure 1-5
Two figures showing alignment between Obelin and Clytin sequences